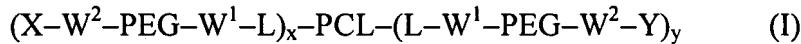


## AMENDMENTS TO THE CLAIMS

1. (Previously presented) A biosensor system for bioassay which comprises, as a set,
  - (A) polyethylene glycol-modified nanoparticles of a structural formula I:



wherein

PCL stands for a free electron metal fine particle, metal oxide fine particle or semiconductor fine particle;

X stands for a functional group or functional moiety capable of binding directly to a biosensor chip surface;

Y stands for at least one group or moiety which is selected from the group consisting of C<sub>1</sub>-C<sub>6</sub> alkyl, a group or moiety defined above as X, and a group or moiety defined above as X which is protected, wherein X and Y are not the same simultaneously;

L stands for a linker group or moiety linked to PCL;

W<sup>1</sup> and W<sup>2</sup> stand for single bonds or same or different linkers, wherein L is different from W<sup>1</sup> and W<sup>2</sup>;

PEG stands for ethylene oxide units, (-CH<sub>2</sub>CH<sub>2</sub>O-)<sub>n</sub>, wherein n is an integer of 5 - 10,000,

W<sup>2</sup>, PEG, W<sup>1</sup> and L in (X-W<sup>2</sup>-PEG-W<sup>1</sup>-L)<sub>x</sub> and (L-W<sup>1</sup>-PEG-W<sup>2</sup>-Y)<sub>y</sub> are same or different, and

x and y are integers of 1 or more independently of each other, which together represent an integer sufficient for the PEG chains to cover the PCL surface in an aqueous medium and

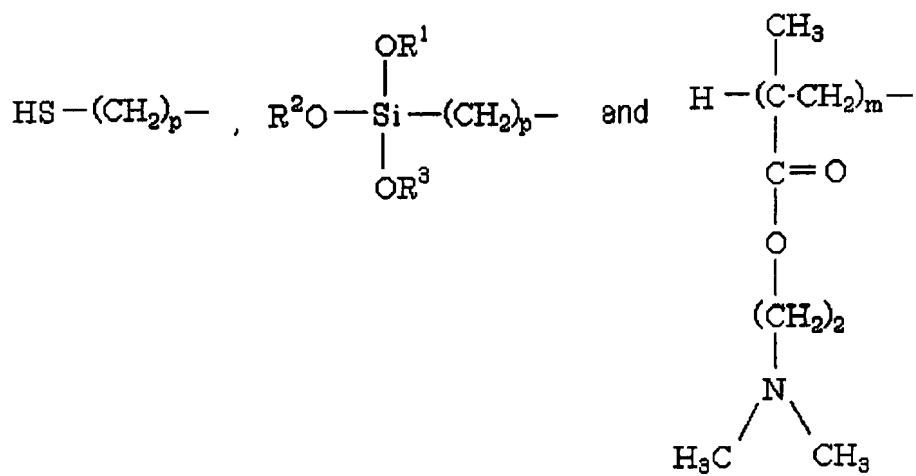
(B) a biosensor chip having a surface to which above (A) particles can bind via X,

wherein X is a residue of a member forming a biological specific binding pair; and

wherein

(B) sensor chip has a thin membrane surface made of a material corresponding to that constituting PCL in the structural formula I, said surface carrying the other member which forms said biological specific binding pair with said member X, either directly or via at least one of C<sub>1</sub>-C<sub>6</sub> alkylene or (-CH<sub>2</sub>CH<sub>2</sub>O-)<sub>n</sub>, wherein n is an integer of 5 - 10,000.

2. (Previously presented) The biosensor system according to Claim 1, wherein said (A) particles are carried on one surface of the (B) biosensor chip as the particles are linked to the biosensor chip surface via X, to substantially cover a part or whole area of said surface.
3. (Previously presented) The biosensor system according to Claim 1, wherein said (A) particles and (B) biosensor chip surface are used in a state of either being capable of binding to each other or being bound, the binding being such that can be replaced by an analyte in an aqueous medium due to competitive action of the analyte.
4. (Currently amended) The biosensor system according to Claim 1, in which –L– in the structural formula I is a group selected from the group consisting of

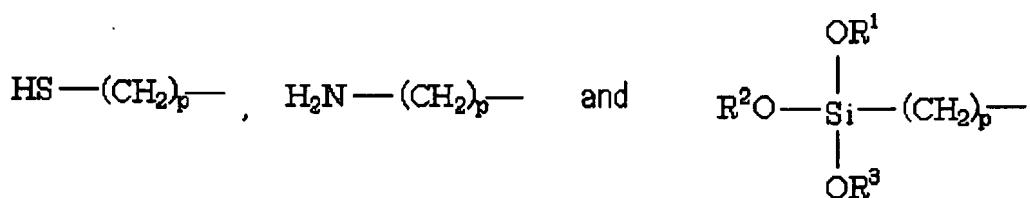


wherein p is independently an integer of 2 – 12, R<sup>1</sup>, R<sup>2</sup> and R<sup>3</sup> each independently stands for C<sub>1</sub>–C<sub>6</sub> alkyl, with the proviso that one of R<sup>1</sup>, R<sup>2</sup> and R<sup>3</sup> is a bond, and m is an integer of 2 - 100; and

W<sup>1</sup> and W<sup>2</sup> each independently stands for a group selected from the group consisting of single bond, C<sub>1</sub>–C<sub>6</sub> alkylene, –COO– (binding to methylene group in ethylene oxide unit via oxygen atom), –O–, –S–, –( C<sub>1</sub>–C<sub>6</sub> alkylene) –COO–, –( C<sub>1</sub>–C<sub>6</sub> alkylene) –O– and –( C<sub>1</sub>–C<sub>6</sub> alkylene) –S–.

5. (Cancelled)

6. (Previously presented) The biosensor system according to Claim 1, wherein X in the structural formula I representing said (A) particle stands for a group selected from the group consisting of

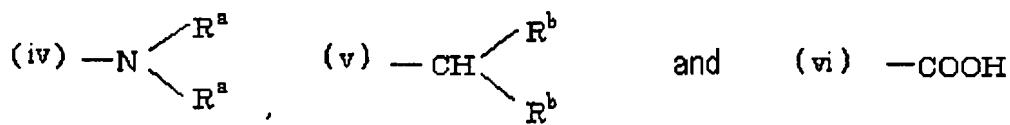


wherein p is an integer of 2 – 12 independently of each other; R<sup>1</sup>, R<sup>2</sup> and R<sup>3</sup> each independently stands for C<sub>1</sub>–C<sub>6</sub> alkyl;

and

said (A) particles and surface of (B) sensor chip are linked to each other via the functional group X.

7. (Previously presented) The biosensor system according to Claim 1, wherein Y in the structural formula I representing said (A) particles is a group selected from the group consisting of:

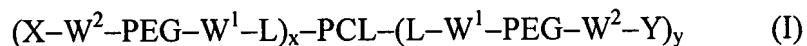


wherein R<sup>a</sup> each independently stands for hydrogen or C<sub>1</sub>–C<sub>6</sub> alkyl; R<sup>b</sup> each independently stands for a C<sub>1</sub>–C<sub>6</sub> alkyloxy; or the two R<sup>b</sup>'s together stand for an atomic group forming oxy or an optionally C<sub>1</sub>–C<sub>6</sub> alkyl-substituted ethylene group.

8. (Previously presented) The biosensor system according to Claim 1, wherein x + y in the structural formula I representing said (A) particles is an integer corresponding to 0.1 – 0.5 per 1 nm<sup>2</sup> of the PCL surface.

9. (Previously presented) The biosensor system according to Claim 1, wherein PCL in said (A) particle has an average cross-sectional length of 5 – 500 nm.

10. (Currently amended) A polyethylene glycol-modified nanoparticle of a structural formula I



wherein

PCL stands for a free electron metal fine particle, metal oxide fine particle or semiconductor fine particle;

X stands for a functional group or functional moiety capable of binding directly to a biosensor chip surface;

Y stands for at least one group or moiety which is selected from the group consisting of C<sub>1</sub>–C<sub>6</sub> alkyl, a group or moiety defined above as X, and a group or moiety defined above as X which is protected, wherein X and Y are not the same simultaneously;

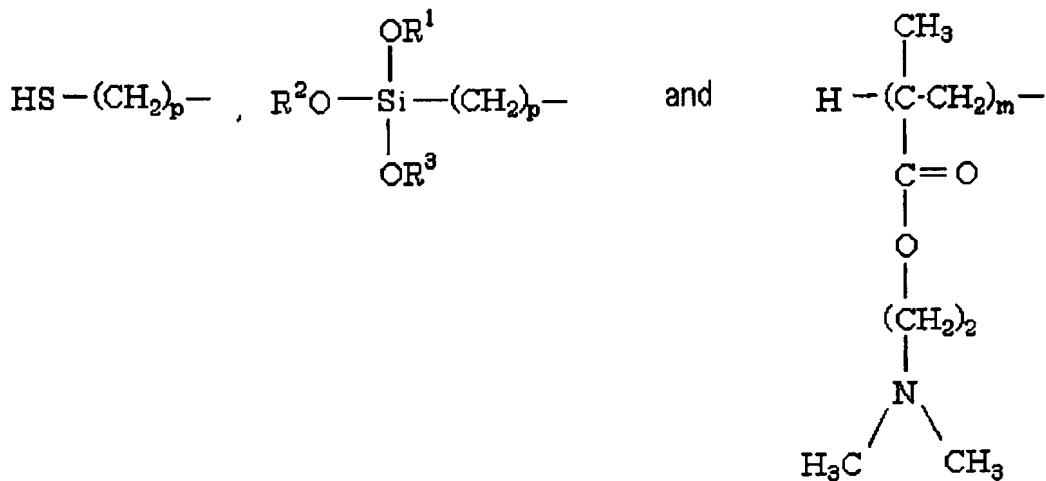
L stands for a linker group or moiety linked to PCL;

W<sup>1</sup> and W<sup>2</sup> stand for single bonds or same or different linkers, wherein L is different from W<sup>1</sup> and W<sup>2</sup>;

PEG stands for ethylene oxide units, (–CH<sub>2</sub>CH<sub>2</sub>O–)<sub>n</sub>, wherein n is an integer of 5 - 10,000,

W<sup>2</sup>, PEG, W<sup>1</sup> and L in (X-W<sup>2</sup>-PEG-W<sup>1</sup>-L)<sub>x</sub> and (L-W<sup>1</sup>-PEG-W<sup>2</sup>-Y)<sub>y</sub> are same or different,

X being a residue of a member to form a biological specific binding pair, Y being a group other than the residue of the member forming said biological specific binding pair, L standing for a group selected from the group consisting of



wherein p is an integer of 2 – 12, R<sup>1</sup>, R<sup>2</sup> and R<sup>3</sup> each independently stands for C<sub>1</sub>–C<sub>6</sub> alkyl, with the proviso that one of R<sup>1</sup>, R<sup>2</sup> and R<sup>3</sup> is a bond, and m is an integer of 2 - 100;

x + y is an integer corresponding to 0.1 – 0.5 per 1 nm<sup>2</sup> of the PCL surface, , (x/ x + y) × 100 being an integer of 20 – 65 and the average dimension of cross-section of the PCL is 5 – 500 nm.

11. (Previously presented) The polyethylene glycol-modified nanoparticle according to Claim 10, wherein said member to form a biological specific binding pair is a residue derived from a substance selected from the group consisting of monosaccharide or oligosaccharide, antigen or hapten, substrate, hormone and oligonucleotide.

12. (Previously presented) A method of detecting an analyte in a biological fluid, which comprises:

- (a) preparing polyethylene glycol-modified nanoparticles as described in Claim 10,
- (b) preparing a biosensor chip having a thin membrane surface made of a material corresponding to that forming PCL of the nanoparticles, said surface carrying, either directly or via at least a C<sub>1</sub>–C<sub>6</sub> alkylene or  $(-\text{CH}_2\text{CH}_2\text{O}-)_n$ , wherein n is an integer of 5 - 10,000, a member which is to form a biological specific binding pair with the other member present in X of said nanoparticles,

- (c) contacting said particles (a) and biosensor chip (b) with a biological fluid which is suspected to contain either one of the members capable of forming the biological specific binding pair as an analyte,

(d) determining the change in the extent of linkage of the particles (a) to the biosensor chip (b) surface caused by the competitive action of the analyte and  
(e) using the change as an index of the analyte concentration in said biological fluid.

13. (Previously presented) The detection method according to Claim 12, wherein the change in the extent of linkage of the particles (a) to the biosensor chip (b) surface in the step (d) is detected as a change in surface plasmon resonance spectrum.

14. (Previously presented) The detection method according to Claim 12, wherein the pair formed by two members capable of forming a biological specific binding pair is selected from the group consisting of sugar - lectin, antigen or hapten - antibody, substrate - enzyme, hormone - receptor protein, and oligonucleotide - either oligonucleotide or polynucleotide which contain complementary chain sequence of the first oligonucleotide.

15. (Previously presented) The detection method according to Claim 12, wherein said particles (a) and the biosensor chip (b) surface form biological specific binding pairs and are linked in advance.

16. (Previously presented) The biosensor system according to Claim 1, wherein n is an integer of 10–10,000, and wherein  $(x/x+y) \times 100$  is an integer of 20–65.

17. (Previously presented) The polyethylene glycol-modified nanoparticle according to Claim 10, wherein n is an integer of 10–10,000.

18. (Previously presented) The detection method according to Claim 12, wherein  $(x/x+y) \times 100$  is an integer of 20–40.